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EXAMINER
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1612

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



## **DETAILED ACTION**

Applicants' arguments, filed 2/12/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections are newly applied. They constitute the complete set presently being applied to the instant application. The previous rejection has been rendered moot by applicant's amendment.

### ***Claim Rejections - 35 USC § 112--New***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 1, 3, 5, 6, 9, 11, 13, 14, 24, 26 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The description requirement of the patent statute requires a description of an

Art Unit: 1612

invention, not an indication of a result that one might achieve if one made that invention. See, e.g., In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984). (Holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.')

Mere indistinct terms (such as "derivative" used herein), however, may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely functional terms. See Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886 (CAFC 2004) at 1892, stating:

The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

Conversely, a description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See Univ. of Calif. V. Eli Lilly, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under Section 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. *If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus*. See MPEP 2163. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the

Art Unit: 1612

disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any *combination of such identifying characteristics that distinguish the claimed invention from other materials* and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Here, the specification does not provide a reasonably representative disclosure of useful acryloyl distamycin derivatives of formula (I) generally, a potentially huge genus inclusive of many different compounds having widely divergent structures and functions. Specifically, the specification discloses only a limited number of species at page 6-7 through line 10, and these are not viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

### **Written Description**

2) Claims 1, 3, 5, 6, 9, 11, 13, 14, 24, 26 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

Art Unit: 1612

inventor(s), at the time the application was filed, had possession of the claimed invention.

The first paragraph of 35 USC 112 requires that the specification contain a written description of *the invention*. Accordingly, where a particular compound has not been *specifically* named or “otherwise exemplified”, one is left to select from mere *possibilities* encompassed by the broad disclosure, with no guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made. In re Ruschig, 154 USPQ 118, 122 (CCPA 1967). As elaborated by the court:

Specific claims to single compounds require reasonably specific supporting disclosure and while we agree with the appellants, as the board did, that *naming* is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required. Surely, given time, a chemist could name (especially with the aid of a computer) all of the half million compounds within the scope of the broadest claim, which claim is supported by the broad disclosure. This does not constitute support for each compound individually when separately claimed.

Here, the instant claim broadly recites “a 5 or 6 membered saturated or unsaturated heterocyclic ring”, but not a specific structure. “Heterocyclic ring” is nominally identified as a 5 or 6 membered saturated or unsaturated. However, there is no definition beyond this. The specification shows examples distamycin compounds of formula (I) at page 6-7 through line 10. However, the heterocyclic ring is not “specifically named or otherwise exemplified”. Accordingly, the claimed subject matter is not adequately described by the specification as originally filed.

***Claim Rejections - 35 USC § 103***

Claims 1-3, 5-9, 11, 13-15 and 24-30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cozzi et al. (WO 98/04524, published February 5, 1998) in view of Cortes et al. (Investigational New Drugs 2000). ***This rejection also applies to claims 31-34.***

Cozzi teaches the acryloyl distamycin derivative of formula I (see page 3 lines 25-30 and page 4 lines 1-5; see also examples that follow pp. 4-7; see also specification at pg. 7, lines 12-16). The compounds are taught to be in association with one or more pharmaceutically acceptable carrier and/or diluent (see col. 18, lines 25-28). Cozzi also discloses that the acryloyl distamycin derivatives can be combined with an additional antitumor agent for treating cancer or for ameliorating the conditions of mammals, including humans, suffering from cancer (see page 20 lines 6-13 and lines 20-29). Combined preparations may be simultaneous, separate or sequential, and are administered "in amounts sufficient to produce a therapeutically useful effect" (see pg. 20, lines 10-13). The reference teaches that the compounds of formula I are useful in treating leukemias (**claim 28**) (see pg. 16, lines 9-12).

Cozzi does not teach a protein kinase inhibitor.

Cortes et al. teach that CGP 57148 (STI 571) is a novel agent that inhibits the tyrosine kinase activity of ABL, and that clinical results suggest a very potent anti-leukemia activity with minimal toxicity in patients with Interferon-resistant Ph-positive CML (see pg. 72, left column, 2<sup>nd</sup> paragraph (II Targeted Therapy)).

Generally, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. See MPEP 2144.06. Thus, combining the acryloyl distamycin compounds of Cozzi with the STI 571 of Cortes as claimed in the instant invention would have been prima facie obvious since they are both taught to be useful for treating leukemia.

### ***Response to Arguments***

Applicant argues that the instant claims are not obvious over Cozzi in view of Cortes, since the *in vitro* data submitted November 7, 2007, shows the synergistic effect of the presently claimed composition. The *in vitro* data (Exhibit I) shows three tables. In each table one compound of formula I (Brostallicin) is combined with either STI571, ZD1839 or OSI-774. The combination of Brostallicin and STI571 was tested against K562 human CML (leukemia) cell line. The combination of Brostallicin and ZD1839 was tested against H322M human lung cancer cell line. The combination of Brostallicin and OSI-774 was tested against MDA-MB-468 human breast carcinoma cell line. The data shows a more than additive effect for each combination.

However, the instant claims are not commensurate in scope with these data. Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In

Art Unit: 1612

other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range.

The instant claims read very broadly, encompassing compounds of the general formula I, which is combined with a protein kinase inhibitor of a Markush group. It is noted that ZD1839 has been deleted from the instant claims. The instant claims are also not limited to a specific type of cancer. The data of Exhibit I do not provide an adequate basis for concluding that the great number of combinations recited in the generic claims would behave in the same way, especially in regard to neoplastic disease states in general. In regard to the *in vivo* method claims, there is also no recitation of concentration ranges or ratios of the combinations that are necessary to produce the same results of the *in vitro* data. Accordingly, the instant claims remain rejected as being obvious over Cozzi in view of Cortes.

***Conclusion***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb  
/Walter E Webb/  
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612